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Letter to the Editor Journal of Clinical Densitometry: Assessment of Skeletal Health

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Dear Dr. Miller

I read with interest the article by Prevrhl and colleagues entitled “Comparison of DXA Hip Structural Analysis with volumetric QCT” and I have some relevant comments.

The paper purports to compare two versions of HSA analyses with geometry derived from CT scans. One version of HSA® is the one I had originally developed (Johns Hopkins University or JHU HSA) (1) and it was compared to an implementation on GE scanners of software based on similar principles and originally developed by Yoshikawa et al(2) (GE HSA). The work was originally presented in oral form at the American Society of Bone and Mineral Research meeting in 2006. At that meeting Dr. Prevrhl presented results showing that there were modest correlations between femoral neck measurements using GE HSA and the femoral neck geometry measured by Dr. Lang’s QCT software, but no significant correlations were evident between JHU HSA and with either GE HSA or the QCT geometry. The result was repeated here with the statement that ‘...the version of the Johns Hopkins HSA program for this particular device was flawed, and we therefore do not present or discuss its results.’ Let me begin by saying that we have no problem with any legitimate comparisons with JHU HSA, regardless of findings, but to make remarks to discredit software that is clearly not working is frankly unprofessional and gratuitous. If our software is ‘flawed’ why it is even mentioned?

As we repeatedly explained to Dr. Prevrhl and colleagues, our HSA method requires a properly calibrated soft-tissue-subtracted image where pixel values are expressed in g/cm² of bone mineral mass. We can derive that image from the data archived by the scanner provided that the scanner manufacturer provides access to their proprietary format and any necessary information needed to produce the mineral image. Over the years we have developed conversion utilities for early Lunar DPA scanners, some Norland models (now Cooper Surgical), all models of Hologic scanners. We also developed conversions for some versions of GE/Lunar DXA models including various versions of the DPX and early versions of the Prodigy used in Dr. Prevrhl’s study. All image conversions were developed using information provided by the manufacturer under non-disclosure agreements. The Prodigy conversion was developed in 2002–2003 in with cooperation with GE. Soon thereafter GE made the business decision to discontinue cooperation with us and to develop geometry software based on the Yoshikawa program. At some point the GE data format was altered; this is clearly the prerogative of the scanner manufacturer to do as their needs dictate and we are under no delusion that GE is required to inform us when they do.. We were nevertheless surprised to

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learn that the modifications to later Prodigy scan data did not prevent our software from working but were more subtle, producing seemingly random errors that took some time for us to discover. JHU did license the software to Synarc in 2005 for use in clinical trials before we were aware of the subtle GE modifications. Although a fine point, the JHU software was provided by Synarc. It was not 'provided by Johns Hopkins University' implying some level of cooperation (which was repeatedly offered) as stated in the paper.

With regard to the specifics of the comparison by Prevrhl and colleagues, I do have some comments and concerns. One might assume that any 3D method is necessarily superior to 2D DXA in the measurement of geometry. This might be the case with current generation multi-row helical CT scanners but for unexplained reasons the authors used a CT scanner model that dates to the early 1990's with a suboptimal helical scan protocol and a section thickness and spacing of 3 mm. As is evident Figure 2 of the paper the image quality in a cross-section is quite poor due to reformatting of the image out of the scan plane. The authors of this publication who have expertise in this area are aware that the section plane resolution as stated in the Materials and Methods is irrelevant for images reformatted out-of-plane with these outmoded protocols. Note that in Figure 2 there are step-like artifacts around the cortical periphery due to aliasing effects resulting from the 3 mm non-overlapped section spacing. In our experience with images provided by Dr. Lang using this protocol the aliasing errors make them unreliable for measuring geometry. The observation that two suboptimal methods provide measurements that correlate is hardly very illuminating given the lack of an absolute standard. It is also curious that a comparison was done between total cross-sectional area and the area of bone within the cross-section. Since there is no obvious relationship between the two the poor correlation is not surprising. While the area within the periosteal contour may be 'purely geometric' only the bone surface within provides mechanical support. The bone surface area can be easily derived from the CT data for a more meaningful comparison and I suspect results would show greater correlations with the GE HSA CSA. Finally the caption on Figure 1 is curious since it refers to the locations of geometry regions crudely corresponding to those of the JHU software (See cover art for that issue) but two of the three regions are apparently not analyzed by the GE version or employed in the paper.

A more appropriate QCT comparison with the HSA methods would analyze the cross-sections in the same femur locations with parameters defined so that they can be directly compared and not merely correlated between differently defined measures. Such a comparison should also employ an absolute geometry standard so that accuracy can be determined. In cooperation with Dr. Keenan Brown of Mindways Software Inc. we have developed geometry algorithms that work well with the higher resolution multi-slice scanners. The software locates cross-sections on the CT data set using the same criteria employed with DXA data and it provides all the same geometric properties in the same measurement units. Moreover bending properties (CSMI and section modulus) are referenced to the frontal plane so they can be directly compared. We have not yet published the method but we showed an in vivo comparison between a 64 slice GE MDCT scanner and JHU HSA using Hologic DXA scans at the 2007 ASBMR meeting(3). In collaboration with Dr. Benjamin Khoo of the University of Western Australia we have also developed a femur geometry phantom to provide an absolute reference standard for both DXA and QCT(4).

There is much to criticize about our HSA® method or any geometry method based on limited 2 dimensional DXA data. I have absolutely no problem with a legitimate comparison, including findings that show errors in our method or that GE HSA or any other method is superior in any respect. A legitimate comparison with GE HSA would of course require cooperation with GE to ensure that images analyzed by our program are properly converted into a format that JHU HSA® can analyze. We are not convinced however that geometry derived by the outmoded QCT protocol is sufficiently reliable for geometry measurements. Since multi-slice scanners

with isotropic spatial resolution are widely available, (several are located at the institution of Drs. Prevrahl and Lang), it makes little sense not to use them for this purpose. Furthermore we would be happy to make our CT software, geometry phantom and calibration capabilities available to Dr. Prevrahl and colleagues for a legitimate comparison between methods.

Sincerely,

Thomas J. Beck

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